

09-29-00

A

LAW OFFICES
NOTARO & MICHALOS P.C.
EMPIRE STATE BUILDING
350 FIFTH AVENUE, SUITE 6902
NEW YORK, NEW YORK 10118-6985
TELEPHONE: 212-564-0200
FAX: 212-564-0217
E-MAIL: nmpe@notaromichalos.com

100 DUTCH HILL ROAD, SUITE
ORANGEBURG, NEW YORK 10962-2119
TELEPHONE: 914-359-7700
FAX: 914-359-7798
PATENTS, TRADEMARKS
COPYRIGHTS

September 28, 2000

VIA EXPRESS MAIL
LABEL NO.: EL 697189949 US

CUSTOMER NO.: 021706

Commissioner for Patents
U.S. Patent and Trademark Office
Washington, D.C. 20231

Attention: Box Patent Applications

Re: TECAN SCHWEIZ AG
U.S. Patent Application
Inventor: Donat Elsener, et al
For : THERMOCYCLER AND LIFTING ELEMENT
Our Ref.: J463-012 US

Sir:

The above-identified utility patent application is
transmitted herewith for filing.

Enclosed are:

1. 10 Page English Appln., including 14 Claims and 1 Pg.
Abstract;
2. 3 Sheets of Drawings, Figs. 1-4b;
3. Declaration and Power of Attorney - Unsigned (3 Pgs.);
4. Preliminary Amendment w/ Ex. Mail ID; and
5. Check - Amt. \$690.00 - No. 3205 (Filing Fee w/o
Assignment - Large Entity).

Commissioner for Patents
September 28, 2000
Page 2

Fee Calculation:

Basic Filing Fee: \$ 690.00

Total No. of Claims Filed: 14 (-20) = x \$18.00

Total No. of Independent
Claims Filed: 1 (- 3) = x \$78.00

Multiple Dependent Claims (if present): \$260.00

Sub-Total: \$ 690.00

SMALL ENTITY (if applicable)

REDUCE FILING FEE BY 50%: \$

Assignment (if applicable): - \$ 40.00

TOTAL FEE: \$ 690.00

Kindly acknowledge receipt of the above items by having your mail room date-stamp and return the attached postcard with a serial number.

Further, the Commissioner is hereby authorized to charge any fee under 37 CFR 1.16 and 1.17 which may be required during the entire pendency of the application to Deposit Account No. 14-1431.

Respectfully submitted,



Peter C. Michalos
Reg. No. 28,643
Attorney for Applicant

(845) 359-7700

Dated: 9/28/00

NOTARO & MICHALOS P.C.
100 Dutch Hill Road
Suite 110
Orangeburg, New York 10962-2100

:al
Attachments

Patent
Atty. Docket: J463-012 US

VIA EXPRESS MAIL
LABEL NO.: EL 697189949 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Donat Elsener, et al
Serial No. : N/A
Filing Date : Concurrently Herewith
Examiner : N/A
Group Art Unit : N/A
For : THERMOCYCLER AND LIFTING ELEMENT

Commissioner for Patents
Washington, D.C. 20231

Attention: Box Patent Applications

PRELIMINARY AMENDMENT

Sir:

Prior to examination, kindly amend the above-identified
application, as follows:

IN THE CLAIMS:

Claim 3, line 1: delete "or 2".

Claim 4, line 1: change "any of Claims 1 to 3" to --Claim
1--.

Claim 5, line 1: change "any of Claims 1 to 4" to --Claim
1--.

Claim 6, line 1: change "Claims 4 and 5" to --Claim 4--.

Claim 7, line 1: delete "any of".

line 2: change "Claims 1 to 6" to --Claim 1--.

Claim 9, line 1: delete "or 8".

Claim 11, line 1: delete "or 10".

Claim 13, line 1: change "any of Claims 7 to 12" to
--Claim 7--.

Claim 14, line 1: change "any of Claims 7 to 13" to
--Claim 7--.

REMARKS

Claims 1-14 are in this application, and presented for the Examiner's consideration.

The claims were amended solely to delete reference to improper multiple dependent claims. No new matter has been added, and entry of this amendment is respectfully requested.

Respectfully submitted,



Peter C. Michalos
Reg. No. 28,643
Attorney for Applicant(s)

(845) 359-7700

Dated: 9/28/00

NOTARO & MICHALOS P.C.
100 Dutch Hill Road
Suite 110
Orangeburg, New York 10962-2100

:al

DESCRIPTION

THERMOCYCLER AND LIFTING ELEMENT

Field of the invention

The invention relates to a thermocycler. Such devices are
5 used for subjecting the content of the wells of microtitre
plates to temperature cycles which initiate specific
chemical reactions. It also relates to lifting elements for
use in thermocyclers.

Prior art

10 In known thermocyclers of the generic type, there is the
problem that the microtitre plate which, in the interests of
good heat transfer, rests closely against the heating
surface frequently becomes baked onto it and can then be
detached from it only with very great difficulty. This
15 either necessitates complicated manipulations or requires
suitable and correspondingly heavy and expensive handling
devices for applying relatively large forces of 150 N or
more. A possible aid is the use of Teflon spray, which can
prevent the microtitre plate from baking on. However, this
20 must be repeated for every plate and complicates the
procedures.

Summary of the invention

It is the object of the invention to improve a known
thermocycler of the generic type so that the microtitre
25 plates can be raised and removed after each treatment
without particular application of force. This object is

achieved by the features in the characterizing clause of Claim 1.

It has been found that, as a result of the measures according to the invention, the microtitre plate is raised
5 after removal of the cover, which permits convenient gripping and lifting thereof without application of force. This may substantially facilitate the manual removal of the microtitre plate, but in particular the removal can also be effected without any manual intervention, by means of
10 handling devices of the type otherwise usual in the laboratory.

Furthermore, the invention provides particularly suitable lifting elements for thermocyclers according to the invention.

15 **Brief description of the drawings**

The invention is explained in more detail below with reference to Figures which show only an embodiment.

Fig. 1 shows a plan view of the heating plate of a thermocycler according to the invention,

20 Fig. 2 shows, on a larger scale, a cut-out from a plan view according to Fig. 1,

Fig. 3 shows a perspective view of a lifting element according to the invention,

Fig. 4a shows a section along IV-IV in Fig. 2, in addition
25 with microtitre plate and cover, and

Fig. 4b shows a section corresponding to Fig. 4a with the cover removed.

Description of the preferred embodiments

The thermocycler, which may be suitable, for example, for holding an 8 x 12 microtitre plate having the dimensions 85 mm x 130 mm, has a heating plate 1 which forms a heating surface 3 which is surrounded by an edge strip 2 and is somewhat higher than said edge strip and in which round indentations 4 are arranged in a regular square grid, each of which indentations is surrounded by an all-round wall 5 (Fig. 2) projecting beyond the base level of the heating surface 3. In each case, a blind hole 6 is provided between four indentations 4.

Six lifting elements 7 are arranged in six of the blind holes 6 altogether, distributed approximately uniformly over the heating surface 3. Each of the lifting elements 7 consists (Fig. 3) of a cylindrical coil spring 8 of stainless steel, the lowermost winding of which is somewhat wider than the other windings, and a contact pin 9 whose approximately cylindrical shaft 10 is inserted into the upper end of the coil spring 8 and is held therein by friction.

The shaft 10 carries an approximately disc-like head 11 which projects laterally from it and against whose lower surface the upper end of the coil spring 8 abuts, while its upper surface forms a round flat abutting surface 12. The contact pin 9 is rotationally symmetrical and is produced as a single piece from a heat-resistant plastic, such as PEEK, PTFE, FP, PPS or PI, for example by the injection moulding process. It may also consist of, for example, ceramic, but

the production is then as a rule more complicated and more expensive. The contact pin 9 is between 3 mm and 8 mm, preferably about 6 mm, long. The diameter of the abutting surface 12 is between 3 mm and 7 mm, preferably about 5 mm.

- 5 The lifting element 7 has a length of between 15 mm and 20 mm, preferably of about 16 mm. Its spring constant in the relaxed position is between 5 N/mm and 7.5 N/mm, in particular 6 N/mm. It is of course also possible to choose other dimensions and properties in adaptation to different
10 designs of the heating plate and depending on the density with which the lifting elements 7 are arranged on the heating surface and which is 1 per 18.4 cm² in the case described above and, as a rule, is at least 1 per 30 cm².

The coil spring 8 is dimensioned in each case so that the
15 somewhat wider lowermost winding is slightly radially compressed in the blind hole 6 so that there is a frictional lock between said winding and the wall of the blind hole 6. The lifting element 7 is thus adequately fixed but can nevertheless easily be removed. The other windings are free
20 from the wall of the blind hole 6 so that the compression of the coil spring 8 is not hindered.

When the thermocycler is used, the microtitre plate 13, which usually consists of plastic, e.g. polypropylene, is placed on the heating surface 3 (Fig. 4a, 4b) manually or
25 preferably by means of a suitable handling device, e.g. a robot arm, and a hinged cover 14 of the thermocycler is lowered onto said microtitre plate so that each of its wells 15 is pressed into a corresponding indentation 4 and rests against its wall (Fig. 4a). This ensures good heat transfer
30 between the heating plate 1 and the samples in the wells 15. The coil springs 8 of the lifting elements 7, which, in the

relaxed state, project about 6 mm above the edges of the walls 5, are compressed by the pressure exerted by the microtitre plate 13 on the abutting surfaces 12 of its contact pins 9 and are shortened by 2 to 3 mm.

5 After the thermal treatment of the samples in the microtitre plate, which, for example to initiate a PCR reaction, may undergo a relatively large number of temperature cycles, each of which may consist of, for example, heating from 4°C to 96°C with subsequent cooling to 4°C, the cover 14 is
10 swivelled up again. Each of the compressed lifting elements 7 exerts an upward force of about 15 N on the microtitre plate 13. This is sufficient to detach the microtitre plate 13 from the heating surface 3 even if it is baked onto the latter and to raise it, possibly with a delay of a few
15 seconds (Fig. 4b). The microtitre plate 13 raised in this manner and no longer connected to the heating surface 3 can now be removed easily and without application of great force, which again can be effected by a robot arm.

It has been found that it is generally sufficient if the
20 lifting elements together exert a force of about 0.8 N/cm², preferably 1 N/cm², on the microtitre plate. Contact pins made of PEEK have proved suitable in that they are thermally stable and do not bake onto microplates of the conventional materials, such as polypropylene, so that the slight
25 frictional lock is sufficient to hold the lifting elements 7 in the blind holes 6.

Apart from the lifting elements 7, the thermocycler can correspond to a known type, e.g. PTC 225 Tetrad from MJ Research, Inc. It is also possible to retrofit known
30 thermocyclers with lifting elements.

List of reference symbols

	1	Heating plate
	2	Edge strip
	3	Heating surface
5	4	Indentation
	5	Wall
	6	Blind hole
	7	Lifting element
	8	Coil spring
10	9	Contact pin
	10	Shaft
	11	Head
	12	Abutting surface
	13	Microtitre plate
15	14	Cover
	15	Well

P A T E N T C L A I M S

1. Thermocycler having a heating plate (1) which forms a heating surface (3) for holding a microtitre plate (13) whose wells (15) are held in indentations (4) provided
5 in the heating surface (3), and having a cover (14) which can be lowered and raised relative to the heating surface (3), **characterized in that** a plurality of elastically compressible lifting elements (7) which, at least when the cover (14) is raised, project beyond the
10 edges of the indentations (4) are distributed over the heating surface (3).
2. Thermocycler according to Claim 1, **characterized in that** the projection of the lifting elements (7) is at least 2 mm, preferably at least 5 mm.
- 15 3. Thermocycler according to Claim 1 or 2, **characterized in that** the density of the lifting elements (7) is at least 1 per 30 cm².
4. Thermocycler according to any of Claims 1 to 3, **characterized in that** each lifting element (7) is
20 removably fixed to the heating surface (3).
5. Thermocycler according to any of Claims 1 to 4, **characterized in that** each lifting element (7) is inserted into a blind hole (6) in the heating surface (3).
- 25 6. Thermocycler according to Claims 4 and 5, **characterized in that** the fixing of the lifting element (7) is effected by frictional locking with the walls of the blind hole (6).

7. Lifting element for a thermocycler according to any of Claims 1 to 6, **characterized in that** it comprises an elongated spring element which is compressible in the longitudinal direction and carries a contact part which
5 forms an abutting surface (12), oriented transversely to the longitudinal direction, at the upper end of the lifting element.
8. Lifting element according to Claim 7, **characterized in that** the contact part consists of plastic, preferably
10 PEEK, PTFE, FP, PPS or PI.
9. Lifting element according to Claim 7 or 8,
characterized in that the spring element is in the form of a coil spring (8) and the contact part is in the form of a contact pin (9) which comprises a shaft (10)
15 surrounded by the upper part of the coil spring (8) and a laterally projecting head (11) which rests on the upper end of the coil spring (8) and whose upper surface forms the abutting surface (12).
10. Lifting element according to Claim 9, **characterized in that**
20 **that** the lowermost winding of the coil spring (8) is somewhat wider.
11. Lifting element according to Claim 9 or 10,
characterized in that the contact pin (9) is rotationally symmetrical.
- 25 12. Lifting element according to Claim 11, **characterized in that** both the shaft (10) and the head (11) of the contact pin (9) are essentially cylindrical.

13. Lifting element according to any of Claims 7. to 12,
characterized in that its length is between 15 mm and
20 mm and the diameter of the abutting surface (12) is
at least 3 mm.
- 5 14. Lifting element according to any of Claims 7 to 13,
characterized in that its spring constant is at least
5 N/mm.

A B S T R A C T

Some of the blind holes (6) between indentations (4) of a heating surface (3) contain lifting elements (7) which, after opening of a cover, release a microtitre plate (13) from the heating surface (3) and raise said microtitre plate about 2 to 3 mm, so that it can be removed without application of force. Each lifting element (7) consists of a coil spring (8) and a contact pin (9) made of, for example, PEEK which is inserted into said coil spring and presses with a round flat abutting surface (12) against the lower surface of the microtitre plate (13). The spring constant of the lifting element (7) is about 6 N/mm.

(Fig. 4b)

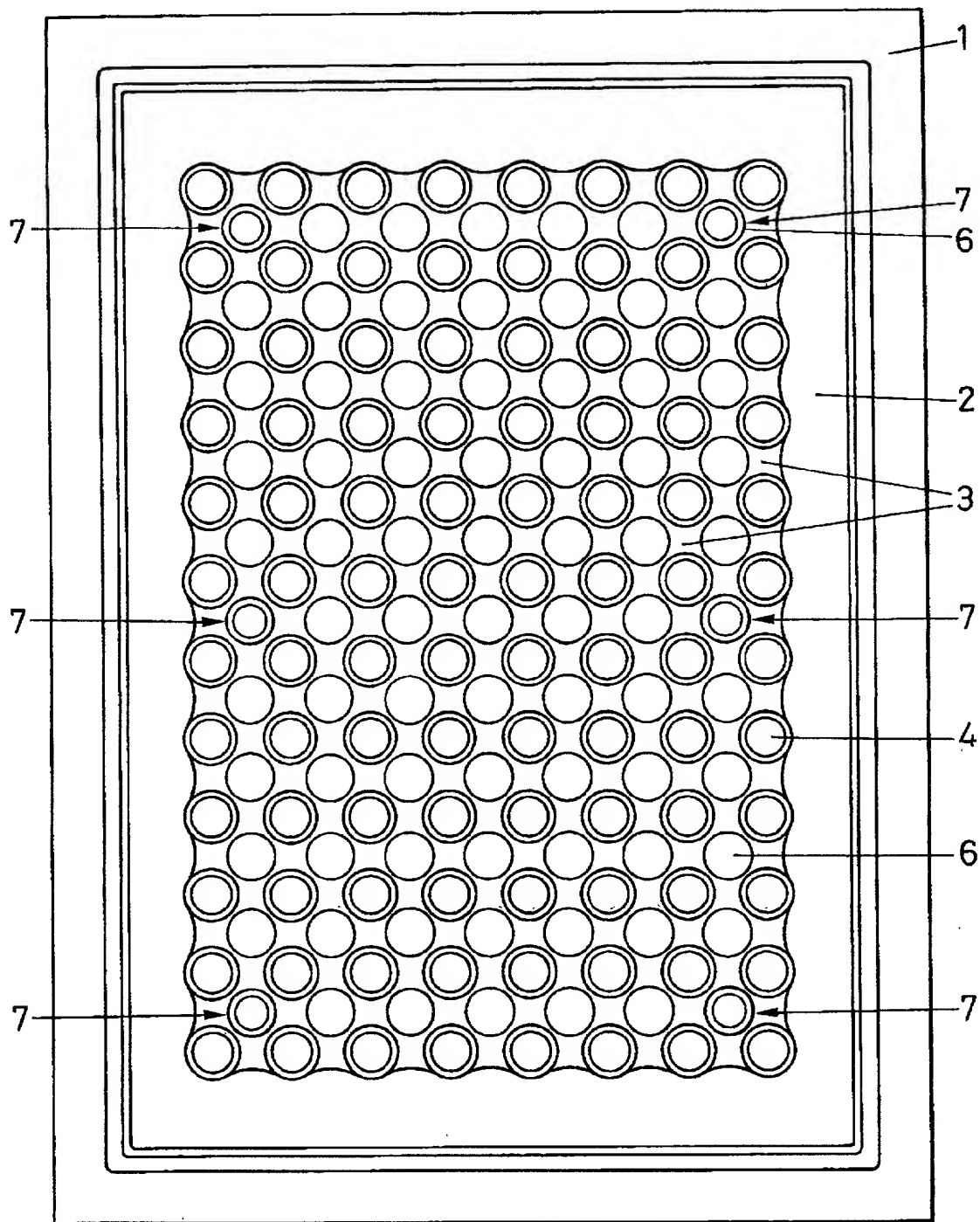
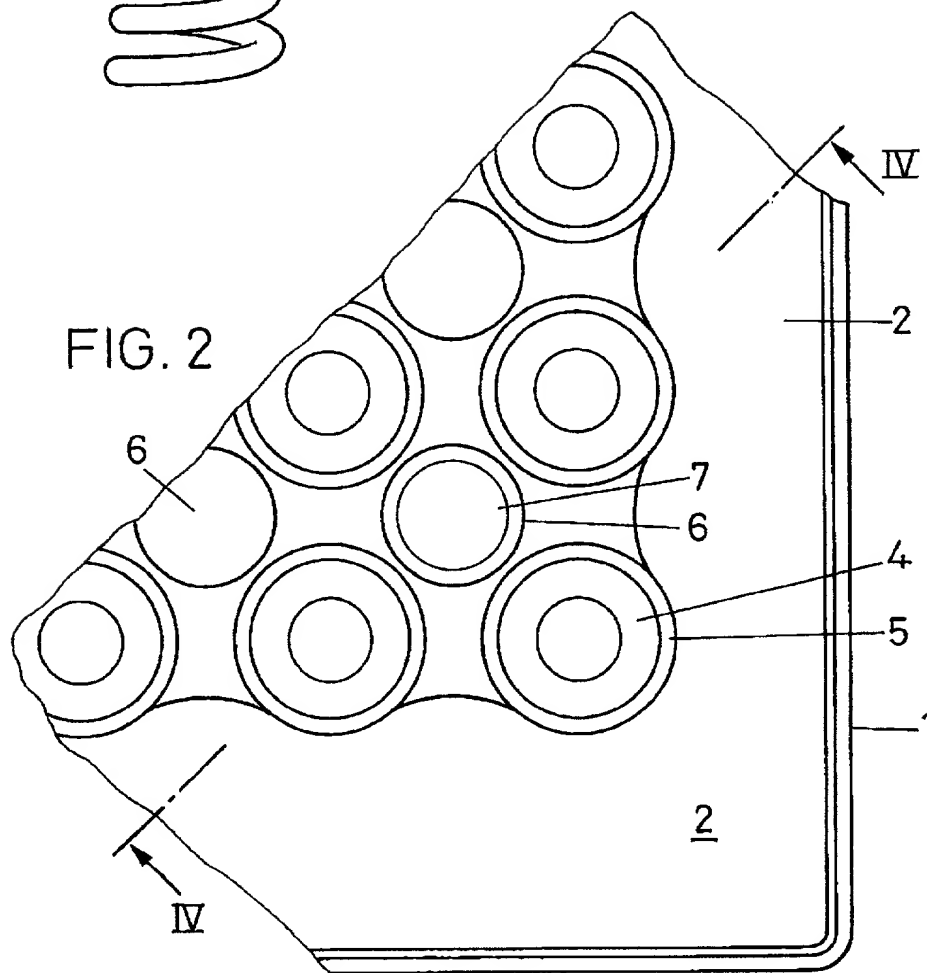
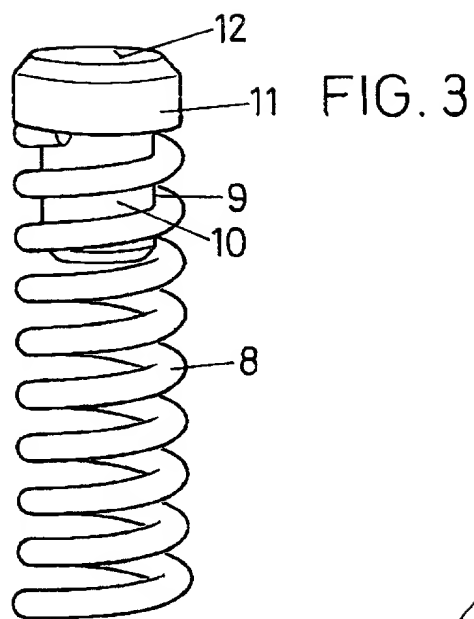
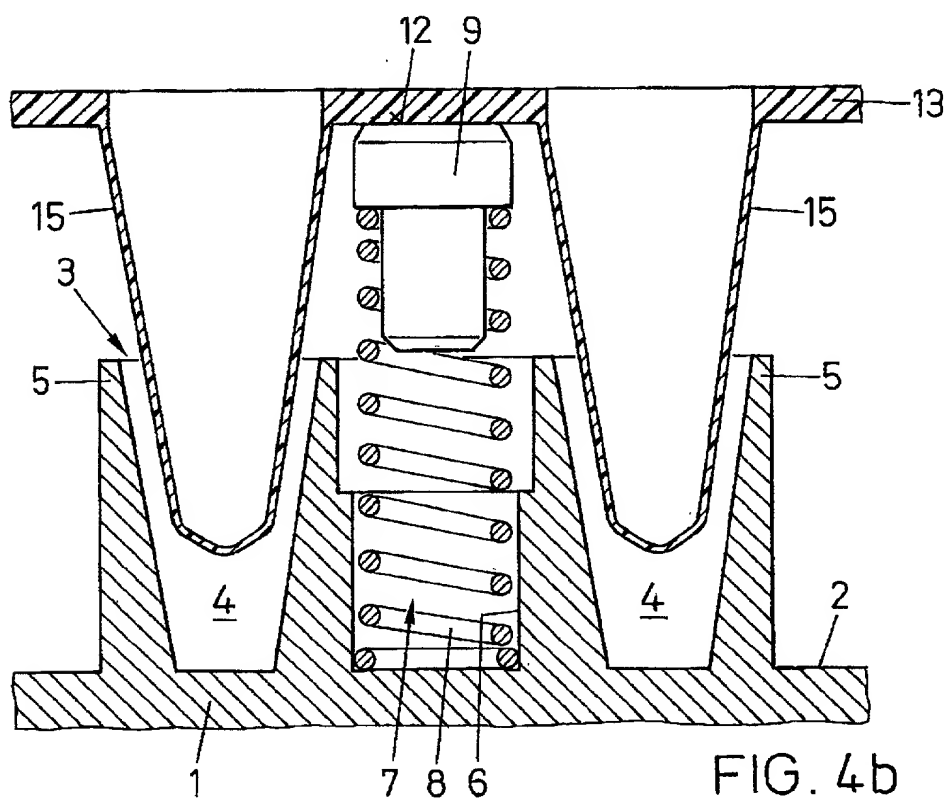
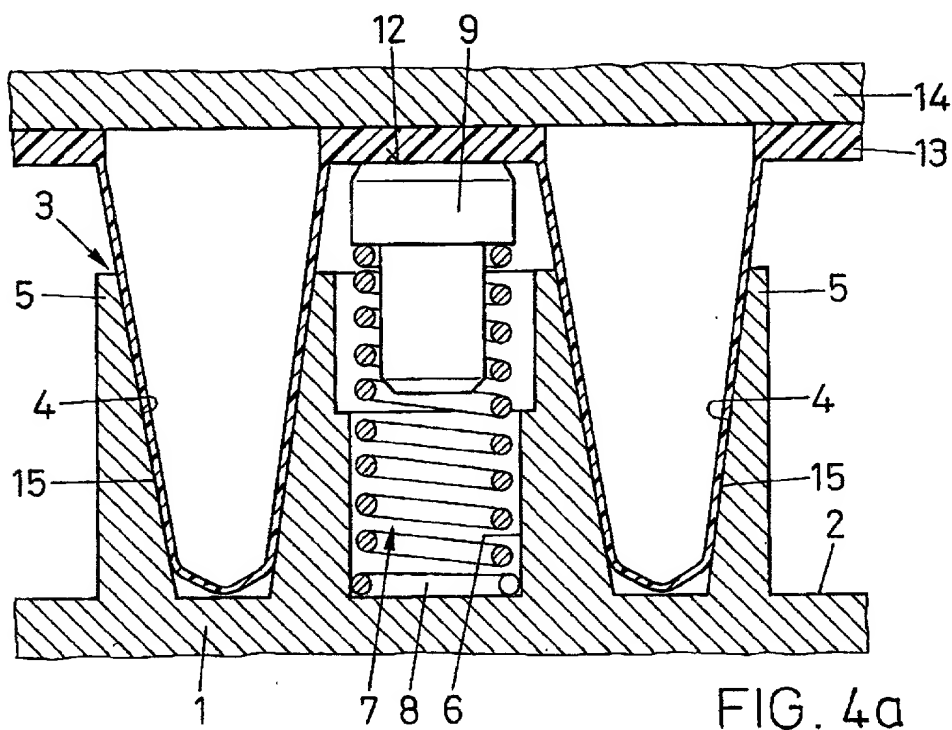


FIG. 1



3/3



**Declaration and Power of Attorney For Patent
Application**

English Language Declaration

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as
stated below next to my name,

I believe I am the original, first and sole inventor (if
only one name is listed below) or an original, first and joint
inventor (if plural names are listed below) of the subject matter
which is claimed and for which a patent is sought on the
invention entitled

THERMOCYCLER AND LIFTING ELEMENT

the specification of which (check one):

☒ is attached hereto
☐ was filed on _____ as
Application Serial No. _____ and
was amended on _____ (if applicable).

I hereby state that I have reviewed and understand the
contents of the above-identified specification, including the
claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is
material to patentability as defined in Title 37, Code of Federal
Regulations, § 1.56.

I hereby claim foreign priority benefits under Title 35,
United States Code, §119 of any foreign application(s) for patent
or inventor's certificate listed below and have also identified
below any foreign application for patent or inventor's
certificate having a filing date before that of the application
on which priority is claimed:

Prior Foreign Applications

Priority Claimed

<u>1782/99</u>	<u>Switzerland</u>	<u>29 September, 1999</u>	Yes	No
(Number)	(Country)	(Day/Month/Year Filed)	[X]	[]
_____	_____	_____	Yes	No
(Number)	(Country)	(Day/Month/Year Filed)	[]	[]

I hereby claim the benefits under Title 35, United States
Code, §119(e) of the following United States Provisional
Application:

Priority Claimed

_____	_____	Yes	No
(Number)	(Day/Month/Year Filed)	[]	[]

Atty. Docket: J463-012 US

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below, and insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

This application is a _____ of U.S. Application

Serial No.	Filing Date	Status (Patented, Pending, Abandoned)
------------	-------------	---------------------------------------

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith.

Angelo Notaro
Reg. No. 27,664

Peter C. Michalos
Reg. No. 28,643

Mark A. Conklin
Reg. No. 39,148

John Zaccaria
Reg. No. 40,241

Martin A. Levitin
Reg. No. 24,479

Send Correspondence to:

NOTARO & MICHALOS P.C.
100 Dutch Hill Road
Suite 110
Orangeburg, New York 10962-2100

Direct Telephone Calls to: (845) 359-7700

Donat ELSENER

Full name of sole or first inventor

Inventor's signature

Date

Mannedorf, Switzerland

Residence

SWISS

Citizenship

Alte Landstrasse 123

CH-8708 Mannedorf, Switzerland

Post Office Address

Atty. Docket: J463-012 US

Daniel RYSER

Full name of second inventor, if any

Inventor's signature

Stafa, Switzerland

Date

Residence

SWISS

Citizenship

Dorfstrasse 27

CH-8712 Stafa, Switzerland

Post Office Address

Full name of third inventor, if any

Inventor's signature

Date

Residence

Citizenship

Post Office Address

Full name of fourth inventor, if any

Inventor's signature

Date

Residence

Citizenship

Post Office Address

Full name of fifth inventor, if any

Inventor's signature

Date

Residence

Citizenship

Post Office Address